REMARKS

Applicant's representative wishes to thank the Examiner for the courtesy extended during the phone interview on April 15, 2008, in which the current amendments to the claims were discussed.

Claims 1-20 and 22-24 are pending herein.

Claims 1, 15, 16 and 18 have been amended to more clearly recite the subject matter of the present invention.

Claims 1 and 18 have been amended to indicate that the immunoglobulin of the present invention is a whole immunoglobulin. Support for this amendment to the claims is found in the specification at Figs. 2 and 4 and the explanation thereof, which states that Fig. 2 shows the SDS-PAGE results of hGH-PEG-IgG conjugates. Clearly, by examining the molar ratio of the various elements of the protein conjugate, it is apparent that the immunoglobulin is whole, and not in fragments.

Claims 15 and 16 are amended to read as originally filed.

Based on the above amendments to the claims and the following remarks, Applicant requests reconsideration and allowance of the instant application.

Amended Claim 1 recites a protein conjugate comprising i) a physiologically active polypeptide ii) a non-peptidic polymer, and iii) a whole immunoglobulin, which are covalently linked to one another, and having a prolonged in vivo half-life of the

physiologically active polypeptide. Amended Claim 18 recites a method of utilizing the protein conjugate of Claim 1.

In the Office Action, the Examiner rejected the claims on the basis of double patenting in view of Application No. 10/535,232. Based on the amendments to the claims, the claims now recite a whole immunoglobulin. Therefore, Applicant submits that the claims of the present invention are patentably distinct from the subject matter and claims of the '232 application. Accordingly, Applicant requests that the claims be allowed and the Application be forwarded to issue.

Claims 1-20 and 22-24 were rejected under 35 USC, 112, first paragraph. Applicant has amended the claims to delete the rejected portion of those claims. Accordingly, Applicant requests that the claims be allowed and the Application be forwarded to issue.

Claims 1-9 and 11-18 were rejected under 35 USC 102(e) as being anticipated by Heavner. As the Examiner recognizes in paragraph 2 of page 5 of the Office Action, Heavner et al. does not require or suggest a whole immunoglobulin. In contrast, the claims as amended recite a whole immunoglobulin. In that regard, we are attaching herewith a document "Kuby Immunology, 4th Edition, page 96" as support of the fact that the immunoglobulin G, employed in the examples of the subject application, has a molecular weight of 150Kda and is a whole immunoglobulin. Therefore, the claims of the present application, as amended, are not anticipated by Heavner. Accordingly, Applicant requests that the claims be

allowed and the Application be forwarded to issue.

Claims 1-2, 9-10, 18-20 and 22 were rejected under 35 USC 102(e) as being anticipated by Mohammed et al. Similar to Heavner, Mohammed also does not require whole immunoglobulin, as the Examiner states on page 6, paragraph 1 of the Office Action. Therefore, the claims of the present application, as amended, are not anticipated by Mohammed. Accordingly, Applicant requests that the claims be allowed and the application be forwarded to issue.

Reconsideration and allowance of claims 1-2, 9-10, 18-20 and 22 is respectfully solicited.

Respectfully submitted,
Attorney for Applicant,

Dated: May 14, 2008

By: _____
Eugene Lieberstein
Registration No. 24,645

CUSTOMER NO.: 79681

BAKER & HOSTETLER, LLP
45 Rockefeller Plaza
New York, NY 10111
Phone: 212-589-4644

CERTIFICATE OF TRANSMISSION

w/attachment

I hereby certify that this Response is being submitted to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 ~~via EFS-Web~~ on May 14, 2008. via U.S. FIRST CLASS MAIL.

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Audrey de Souza

KUBY

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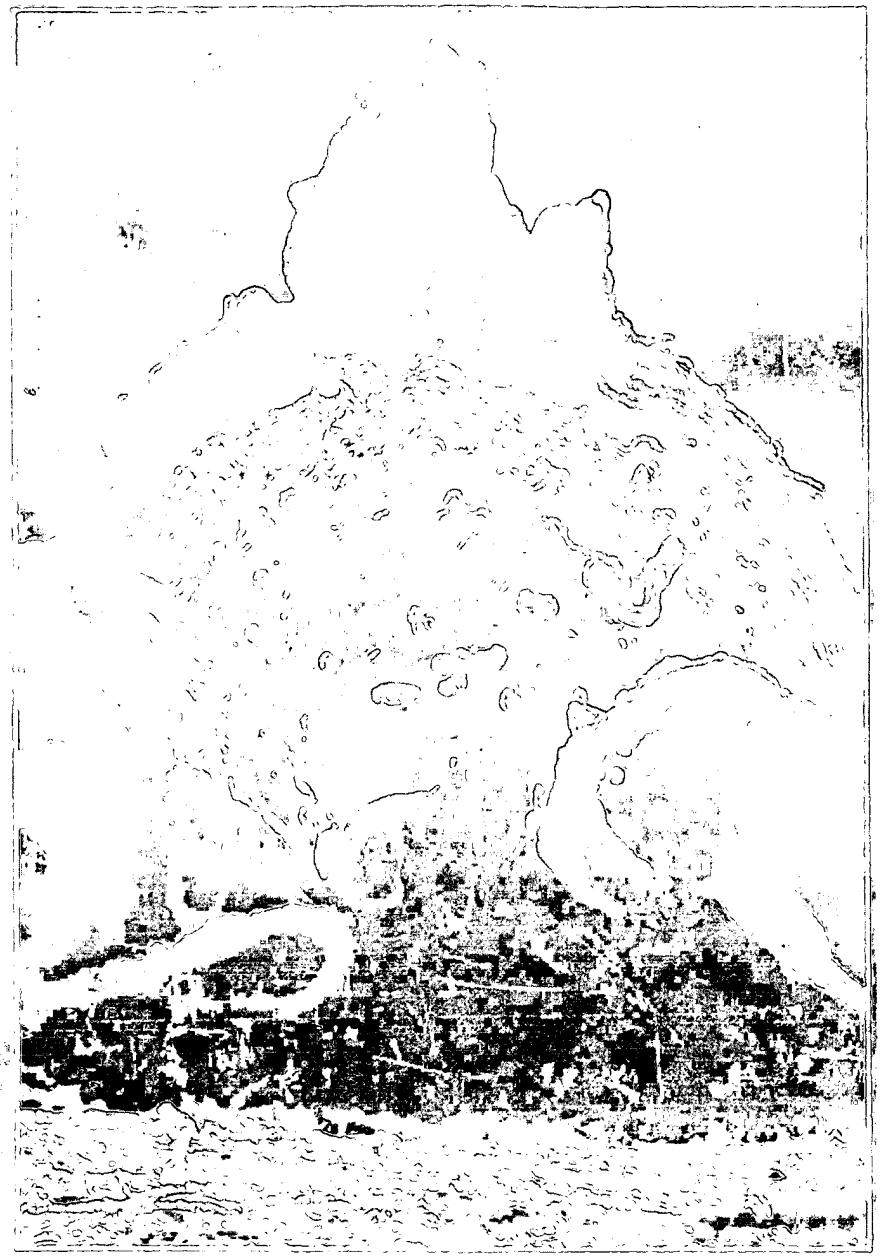

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TABLE 4-2 PROPERTIES AND BIOLOGICAL ACTIVITIES* OF CLASSES AND SUBCLASSES OF HUMAN SERUM IMMUNOGLOBULINS

Property/Activity	IgG1	IgG2	IgG3	IgG4	IgA1	IgA2	IgM†	IgE	IgD
Molecular weight‡	150,000	150,000	150,000	150,000	150,000–600,000	150,000–600,000	900,000	190,000	150,000
Heavy-chain component	γ1	γ2	γ3	γ4	α1	α2	μ	ε	δ
Normal serum level (mg/ml)	9	3	1	0.5	3.0	0.5	1.5	0.0003	0.03
In vivo serum half life (days)	23	23	8	23	6	6	5	2.5	3
Activates classical complement pathway	+	+/−	++	−	−	−	+++	−	−
Crosses placenta	+	+/−	+	+	−	−	−	−	−
Present on membrane of mature B cells	−	−	−	−	−	−	+	−	+
Binds to Fc receptors of phagocytes	++	+/−	++	+	−	−	?	−	−
Mucosal transport	−	−	−	−	++	++	+	−	−
Induces mast-cell degranulation	−	−	−	−	−	−	−	+	−

*Activity levels indicated as follows: ++ = high; + = moderate; +/− = minimal; − = none; ? = questionable.

†IgG, IgE, and IgD always exist as monomers; IgA can exist as a monomer, dimer, trimer, or tetramer. Membrane-bound IgM is a monomer, but secreted IgM in serum is a pentamer.

‡IgM is the first isotype produced by the neonate and during a primary immune response.

Activation of Complement

IgM and, in humans, most IgG subclasses can activate a collection of serum glycoproteins called the **complement system**. Complement includes a collection of proteins that can perforate cell membranes. An important byproduct of complement activation pathway is the protein fragment called C3b, which binds nonspecifically to cell- and antigen-antibody complexes near the site of activation. Many cell types—for example, red blood cells and macrophages—have receptors for C3b and so bind cells or complexes to which C3b has adhered. Binding of adherent C3b by macrophages leads to phagocytosis of the cells or molecular complexes attached to C3b. Binding of antigen-antibody complexes by the C3b receptors of a red blood cell allows the erythrocyte to deliver the complexes to liver or spleen, where resident macrophages remove them without destroying the red cell. The collaboration between antibody and the complement system is important for the inactivation and removal of antigens and the killing of pathogens. The process of complement activation is described in detail in Chapter 13.

Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)

The linking of antibody bound to target cells (virus infected cells of the host) with the Fc receptors of NK cells can kill the cell. In this process, called ADCC, the NK cell causes death by apoptosis of the target cell.

Transcytosis

The delivery of antibody to the mucosal surfaces of the respiratory, gastrointestinal, and urogenital tracts, as well as its export to breast milk, requires the movement of immunoglobulin across epithelial layers. The capacity to be transported depends upon properties of the constant region. In humans and mice, although IgM can be transported to mucosal surfaces, IgA is the major antibody species that undergoes such **transcytosis**. Some mammalian species, for example humans and mice, also transfer significant amounts of most subclasses of IgG from mother to fetus.